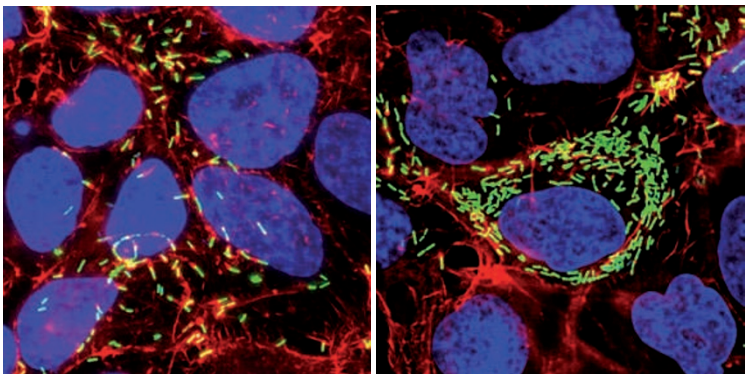
BACTERIAL PATHOGENESIS

A 'hijacked' regulatory mechanism

To disseminate between host cells, *Listeria monocytogenes* polymerizes host cell actin using ActA, a bacterial protein that mimics the action of Wiscott–Aldrich syndrome protein (WASP) and recruits the actin-nucleating ARP2/3 complex to the bacterial surface. This results in the formation of actin tails, which are required for cell-to-cell migration. A study by Chong *et al.* now reveals that, in addition to mimicking the host cell protein, *L. monocytogenes* 'hijacks' the host cell mechanism that regulates this process.



Control (left) and CSNK2B-depleted (right) cells infected with *L. monocytogenes* expressing green fluorescent protein and stained for filamentous actin (red); host cell nuclei are stained in blue. Bacteria infecting CSNK2B-depleted cells show defects in cell-to-cell spread and do not associate with actin. Image courtesy of R. Chong, Yale University School of Medicine, USA.

In host cells, phosphorylation of the verprolin–cofilin–acidic (VCA) domain of WASP by the serine/threonine protein kinase CK2 (casein kinase 2) is required for its interaction with the ARP2/3 complex and subsequent actin polymerization. Preliminary screens identified *CSNK2B* (which encodes the regulatory β-subunit of CK2) as a candidate gene involved in *L. monocytogenes* cell-to-cell spread. On the basis of these data, the authors examined whether CK2 has a role in *L. monocytogenes* dissemination. They depleted CSNK2B from the host cells using small interfering RNA and observed that the absence of CSNK2B significantly impaired bacterial cell-to-cell spread. Furthermore, depletion of CSNK2B inhibited the association of *L. monocytogenes* with host cell actin and the formation of long actin tails.

As ActA has a region that is similar to the VCA domain of WASP, the authors investigated whether this region also has CK2 phosphorylation sites. Indeed, mutation of two serine residues in this region decreased CK2-mediated phosphorylation. Furthermore, mutation of both serine residues resulted in reduced *L. monocytogenes* cell-to-cell spread and a defect in actin tail formation. This phenotype was partially rescued in bacteria with mutations that mimic phosphorylation, confirming that phosphorylation of these residues is necessary for actin tail formation.

So does CK2 phosphorylation of *L. monocytogenes* ActA mediate the interaction of ActA with the ARP2/3 complex, similarly to what is observed in host cells? *In vitro* assays showed that phosphorylation of ActA by CK2 markedly increased the interaction of ActA with the ARP2/3 complex. This depended on phosphorylation of the serine residues in the corresponding VCA domain of ActA by CK2, as their mutation abrogated ARP2/3 recruitment to the bacterial cell surface. Finally, mutation of these residues resulted in an attenuation of spleen colonization in an *in vivo* mouse model of *L. monocytogenes* infection, confirming the importance of ActA phosphorylation by CK2 in *L. monocytogenes* cell-to-cell spread.

Taken together, these findings show that phosphorylation of ActA by CK2 mediates ActA binding to ARP2/3 and results in actin tail formation and consequent *L. monocytogenes* cell-to-cell spread. So, in addition to hijacking the structure of the VCA domain, *L. monocytogenes* has co-opted the mechanism by which the host cell regulates actin polymerization in a case of regulatory mimicry.

Rachel David

> "*L. monocytogenes* has co-opted the mechanism by which the host cell regulates actin polymerization"

ORIGINAL RESEARCH PAPER Chong, R. *et al.* Regulatory mimicry in *Listeria monocytogenes* actin-based motility. *Cell Host Microbe* **6**, 268–278 (2009)

FURTHER READING Elde, N. C. & Malik, H. S. The evolutionary conundrum of pathogen mimicry. *Nature Rev. Microbiol.* **7**, 787–797 (2009).